Syngenta/State of Oregon and Region 10 Federal Agency Meeting
Friday, September 23, 2011
3pm to 5pm
Portland Marriott City Center
List of Attendees

1. **Gail Shibley**, Administrator for Oregon Environmental Public Health, Oregon Health Authority (OHA)

2. **Jae Douglas**, Research & Education Services Section Manager, OHA, Epidemiologist, Pesticide Analytical Response Center (PARC) co-chair

3. **David Farrer**, Toxicologist, Office of Environmental Public Health, OHA

4. *Sujata Joshi, Epidemiologist for the Oregon Public Health Environmental Health Assessment Program, OHA – TENTATIVE*

5. **Lisa Hanson**, Deputy Director, Oregon Department of Agriculture (ODA)

6. **Dale Mitchell**, Assistant Administrator, Pesticides Division, ODA, PARC co-chair

7. **Mike Odenthal**, Lead Investigator – ODA/PARC

8. **Elizabeth Allen**, Toxicologist, Risk Evaluation Unit, EPA Region 10

9. **Kay Morrison**, Public Affairs, EPA, Region 10

10. **Dr. Karen Larson**, Toxicologist, Regional Representative, ATSDR Region 10

11. **Aaron Borisenko**, Laboratory Staff, Watershed Assessment, Oregon Department of Environmental Quality (DEQ)

12. **Kevin Masterson,** Agency Toxics Coordinator, DEQ

13. **Jeff Jenkins, Ph.D.,** Environmental & Molecular Toxicology Department, Oregon State University, PARC consultant

14. **Fred Berman, D.V.M. Ph.D.,** Director, Toxicology Info Center, Center for Research on Occupational and Environmental Toxicology (CROET), Oregon Health Sciences University, PARC consultant – by teleconference

15. **Daniel Sudakin, MD, MPH**, Environmental & Molecular Toxicology Department, Oregon State University – PARC consultant – by teleconference

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A Quantitative Tool for Predicting Human Biomonitoring Results for Atrazine Based On Human Pharmacokinetic Data and Exposure Databases

Final Report

DATA REQUIREMENT(S):	Not Applicable
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NOTE: This report contains color page(s).

VOLUME 1 OF 1 OF STUDY

PAGE 1 OF 34

1.0 SUMMARY OF MATERIAL FOR DISCUSSION ON SEPT. 23RD

The purpose of this document is

1) To summarize the rodent, monkey and human pharmacokinetic parameters for atrazine and its chlorotriazine metabolites.

2) To provide estimates of the magnitude of potential exposure to atrazine and/or its chlorometabolites via diet, in drinking water, from dermal exposure after aerial application and inhalation exposure to volatile or respirable particles.

3) To describe a **preliminary quantitative tool** for estimating the concentration of chlorotriazines that may occur in human urine following exposure to atrazine (Appendix A).

Common Mechanism of Toxicity Group

- The common mechanism of toxicity group for the chlorotriazine herbicides, registered in the United States, is comprised of atrazine (ATZ), simazine, propazine and their chlorometabolites including de-ethyl atrazine (DEA), de-isopropyl atrazine (DIA) and diaminochlorotriazine (DACT) (Figure 1; USEPA, 2002).
- Glutathione conjugates (Figure 2) and metabolites downstream from glutathione conjugation (mercapturates, sulfhydryls and disulfides) are not included in the common mechanism group (USEPA, 2002).
- Primary plant metabolites, the hydroxyatrazine metabolites (Simoneaux and Gould, 2008) are also excluded because these metabolites are considered to have a differ mechanism of action (USEPA, 2002).

Atrazine is Rapidly Metabolized and Cleared from Plasma in the Rat

- Following a single oral dose of atrazine, maximum plasma concentrations of ATZ, DEA and DIA are achieved within 0.4 to 1.25 hours depending on the dose for atrazine, DEA, and DIA and within 1.25 to 8 hours depending on dose for DACT (Table 1; Figure 3; Coder et al., 2011).

- Because of the rapid pharmacokinetics, 90% of steady state concentration was achieved only for DACT after 1, 3 or 11 hours depending on dose.

^{14}C Atrazine is Rapidly Metabolized, Cleared from Plasma, and Eliminated in Urine in Non-Human Primate

- Studies in rhesus (Hui et al., 1996a) and cynomolgus monkeys (Stuhler, 2011; study ongoing) indicate that ^{14}C atrazine equivalents are rapidly cleared from plasma and eliminated in urine (~85%) and feces (~12%; Hui et al., 1996a).

- The half-life of plasma clearance of ^{14}C atrazine equivalents in rhesus monkeys estimated from a two-compartment pharmacokinetic model was 1.5 and 17.7 hours (Figure 4; Hui et al., 1996a).

- The half-life for elimination of ^{14}C atrazine equivalents in urine was 20.8 hours (Hui et al., 1996a).

Atrazine's Chlorometabolites are Rapidly Eliminated in Urine by Humans

- In a human study conducted by Syngenta, 6 men who received a single oral dose of 0.1 mg/kg atrazine, eliminated an average 7.7% of the dose as DACT, 1.4% as DIA, 5.3% as DEA and 0% as ATZ (not detected) over 7 days (Cheung, 1990).

- The average half-life for urinary elimination of DACT, which was best described by a single compartment, first order elimination model, was 11.5 hours.

- The concentration of DACT in urine declined in a log linear manner to non-detectable levels by 96 hours.

- The elimination of DIA and DEA had a fast and a slow component. The half-lives for the fast component were 2.3 and 2.4 hours for DIA and DEA, respectively.

- The half-lives for the slow phase were 8.4 and 36.2 hours for DIA and DEA, respectively.

Models of the Urinary Elimination of Chlorotriazines in Humans

Physiologically Based Pharmacokinetic (PBPK) Model

- The McMullin (2003) PBPK model has been re-parameterized (Campbell et al., 2011) based upon
  - New *in vivo* rodent kinetic data (Coder et al., 2011) and

- New *in vitro* data describing the oxidative metabolism of atrazine to DEA, DIA and DACT by rat and human hepatocytes (Figure 5; Kim et al., 2010; Thomas, 2011). (Note that the rat hepatocytes preferentially N-dealkylate atrazine to DIA whereas human hepatocytes preferentially form DEA).

- The rate of formation and clearance from plasma of the oxidative, the sulfhydryl, and the glutathione conjugated metabolites and the mercapturates of atrazine, DEA, DIA and DACT is being characterized in cynomolgus monkey (Stuhler, 2011; Barr, 2011a).

- A PBPK model describing the elimination of chlorotriazines in the urine of humans (Campbell et al., 2011) is being developed based upon the rodent data (Coder et al, 2011; Thomas 2010) and the ongoing study in female cynomologus monkey (Stuhler et al., 2011; Barr, 2011a). Preliminary results indicate that predictions of levels of DEA, DIA and DACT in human urine derived from the PBPK model are comparable to the spreadsheet calculator as described below.

Forward- and Back-Calculator Tool

- A spreadsheet calculator was developed based upon the characterization of the urinary elimination of DACT (Figure 6), DEA (Figure 7) and DIA (Figure 8) in humans (Cheung, 1990).

- In the Foward-Calculation mode, the calculator requires that the user provides estimates of exposure to atrazine (diet, drinking water, dermal, inhalation) and the calculator returns urinary concentrations of DEA, DIA and DACT at selected durations of time after exposure (See Appendix A for the User's Guide to the calculator).

- In the Back-Calculation mode, urine concentration of DEA, DIA or DACT can be entered and the calculator determines the amount of atrazine required in diet, water, air or via occupational exposure to give the specified level of the metabolite in urine.

- Potential exposure inputs to the calculator are discussed in the following section and appropriate sections appear as worksheets in the calculator.

Potential Exposure to Atrazine via Drinking Water

- Monitoring data collected under the Safe Drinking Water Act (SDWA) indicate that the US population is minimally exposed to atrazine. 93.53% of 142,595 samples analyzed for atrazine during the period from 2001 to 2009 were below the Limit of Detection (LOD) (Breckenridge et al., 2011).

- No detectable residues of either atrazine or simazine were reported in 206 water samples analyzed for a SDWA-based monitoring program in Lane County, Oregon from 2003 to 2008 (http://170.104.63.9).

- One atrazine detect (0.32 ppb, City of Vale in Eastern Oregon) was reported out of 2,644 atrazine samples analyzed in the state wide SDWA compliance monitoring program for Oregon from 2001 to 2008 (http://170.104.63.9).

- Syngenta's frequent monitoring programs for vulnerable Community Water Systems (CWSs), summarized in Figure 9, provide a large historical database (42,131 samples analyzed from 2006 to 2010 for continental United States (Distribution of results shown in Figure 9).

- Only 1 Community Water System (CWS) out of 149 evaluated exceeded the 90 day rolling average of 12.5 ppb total chlorotriazine in 1 year (Sielken, 2011). The EPA (USEPA, 2006) used the 12.5 ppb 90-day rolling average concentration as a level of concern in the Reregistration Eligibility Decision (RED) assessment for atrazine.

Chlorotriazine Exposure via Diet

- Tolerances have been established by the USEPA for atrazine and its chlorotriazine residues on various feed and food commodities (Table 2).

- The USDA's Pesticide Data Program (2009) report indicates that atrazine and its metabolites are rarely detected in food commodities.

- An assessment by Syngenta (Bray et al., 2001) and the USEPA (USEPA, 2006), indicate that exposure to atrazine and its chlorometabolites is small (5×10^{-6} mg/kg). This dose represents only 0.3% of the chronic reference dose for the chlorotriazines.

Dermal and Inhalation Exposure to Atrazine During/After Application

- The dermal penetration of atrazine has been determined in humans and range from 1.2% to 5.6% of applied dose after 24 hours (Hui et al., 1996b).

- Occupational exposure of agricultural workers who handled or applied atrazine to corn and sorghum has been assessed based upon
    1) the Pesticide Handler's Exposure Database (PHED; Selman, 1996)
    2) whole body dosimeters (Lunchick and Selman,1998)
    3) biomonitoring (Lunchick and Selman,1998; Selman,1998).

- Estimated daily dose of atrazine for flaggers potentially exposed to atrazine following aerial application to corn, sorghum and as part of vegetative management programs derived from the Pesticide Handlers Exposure Database (Selman, 1995) represent an extreme upper bound estimate of potential bystander exposure.

Off-Target Transport in the Environment
Volatilization vs. Particulate Concentrations of Atrazine

- Based upon the vapour pressure for atrazine of 3×10^{-7} mm Hg at 20°C, the saturated vapour concentration of atrazine at 20°C was calculated to be 2.9×10^{-9} (i.e. ppb mass fraction) which is equivalent to 3.5×10^{-3} μg/L.

- Yao et al., (2008), who determined the gas and particulate phase concentrations of atrazine in Canadian agricultural regions during the use season, reported up to 985 pg/m^3 atrazine in the vapour phase and 51 pg/m^3 in the particulate phase (Figure 10). Hayward (2010) reported similar levels (Figure 11).

- Assuming that the results presented by Yao et al. (2008) are valid, then the sum of the particulate and vapour concentrations (1.04×10^{-6} ug/L), when utilized as an input to the biomonitoring calculator, are predicted to result in non-detectable levels of DACT in urine (0.4 ppt 12 hours post-exposure).

Concentrations of Atrazine in Rainwater

- Atrazine has been reported in rainwater in various agricultural regions of the United States at median concentrations ranging from 0.014 to 0.053 ppb (Vogel et al., 2008).

- Atrazine levels of 0.015 to 0.060 ppb have been reported in high elevation National Parks in the Western United States (Mast, 2007).

- Atrazine concentration in rainfall is not expected to contribute significantly to human exposure because the levels appearing in rainfall are well below the MCL of 3 ppb.

2.0 BIOMONITORING EQUIVALENTS FOR ATRAZINE

- It has recently been suggested that references doses of chemicals should be re-expressed in terms of biomonitoring equivalent (BME) concentrations in urine (Hays et al., 2008a) and guidelines for accomplishing this have been developed (Hays et al., 2008b).

- The calculator that we have described herein is a first step to developing a BME for atrazine and the atrazine PBPK model will provide a further refinement of such calculations.

3.0 CONCLUSIONS

- There is sufficient information from animal and human studies to reliably predict the concentration of DEA, DIA and DACT in urine following a single dose exposure to atrazine.

- There is sufficient information from animal models to predict steady state concentrations of the chlorotriazine in plasma and urine following repeated daily exposure to atrazine, DEA, DIA and DACT.

- The Forward-Calculator Tool can be used to predict urinary concentrations of DEA, DIA or DACT following potential exposure to atrazine in diet, water, air or dermally.

- The Back-Calculator Tool can be used to back calculate exposure inputs in diet, water, air or by the dermal route needed to support measured concentrations of DEA, DIA or DACT in urine.

- The PBPK model will provide a refined method for dynamically predicting plasma and urinary concentrations of the chlorotriazine. This model is capable of accepting highly resolved temporal dose inputs of ATZ, DEA, DIA and DACT.

- This program of research will permit the establishment of an accurate and reliable BME concentrations for atrazine and its chlorometabolites.

4.0 REFERENCES

Barr, D.B. and Panuwet, P., (2011). Assessing atrazine and its metabolites in non-human primates treated with atrazine. Final Protocol Date: April 7, 2011.

Barr, D.B. Pesticides Exposures: Are we adequately protecting our children. Presentation to Oregon Department of Forestry. April 29, 2011.

Bray, L.D., Beidler, W.T. and Szarka, A. (2001). Chronic Dietary Exposure Assessment for Atrazine and the Simazine metabolites common to Atrazine. Syngenta Study Number 1256-00, April 11, 2001.

Breckenridge, C.B. Christensen, B., and Dando, C. (2011). Safe Drinking Water Act Atrazine Compliance Monitoring at Community Water Systems in the United States from 2001 to 2009. Final Report, July 19.

TABLE 2 **Residue Tolerances for the Combined Residues of Atrazine, DEA, DIA and DACT on Feed and Fed Commodities (Code of Federal Regulations (CRF Section 180.220)**

§ 180.220 Atrazine; tolerances for residues.

(a) *General*. Tolerances are established for the combined residues of the herbicide atrazine (2-chloro-4-ethylamino-6-isopropylamino-s-triazine) and its chlorinated metabolites 2-amino-4-chloro-6-isopropylamino-s-triazine, 2-amino-4-chloro-6-ethylamino-s-triazine, and 2,4-diamino-6-chloro-s-triazine, in or on the following food commodities:

Commodity	Parts per million
Cattle, fat	0.02
Cattle, meat	0.02
Cattle, meat byproducts	0.02
Corn, field, forage	15
Corn, field, grain	0.20
Corn, field, stover	0.5
Corn, pop, forage	1.5
Corn, pop, grain	0.20
Corn, pop, stover	0.5
Corn, sweet, forage	15
Corn, sweet, kernel plus cob with husks removed	0.20
Corn, sweet, stover	2.0
Goat, fat	0.02
Goat, meat	0.02
Goat, meat byproducts	0.02
Grass, forage	4.0
Grass, hay	4.0
Guava	0.05
Horse, fat	0.02
Horse, meat	0.02
Horse, meat byproducts	0.02
Milk	0.02
Nut, macadamia	0.20
Sheep, fat	0.02
Sheep, meat	0.02
Sheep, meat byproducts	0.02
Sorghum, forage, forage	15
Sorghum, grain forage	15
Sorghum, grain, grain	0.20
Sorghum, grain, stover	0.50
Sugarcane, cane	0.20
Wheat, forage	1.5
Wheat, grain	0.10
Wheat, hay	5.0
Wheat, straw	0.50

Appendix 1 User's Guide to the Chlorotriazine Urinary Concentration Forward- and Back-Calculator

1. Summary

The Forward Calculator Worksheet (Forward-Calc UrineConcALLroutes) allows the user to input exposure information for four routes of exposure [dietary, water ingestion, air inhalation and worker exposure (or dermal contact)]. The worksheet then calculates the urine concentrations of DACT, DEA and DIA that would result after a specified number of hours from the time of the dosing.

The Back-Calculator Worksheet (Back-Calc HalfLifeHours) allows the user to specify the urine concentration of any one of the three chlorometabolites, DACT, DEA, or DIA. The worksheet calculates the amount (mg) of atrazine that would have to have been necessary in order to result in the specified urine concentration(s).

Both the Forward- and Back-Calculator Worksheets assume that the percentages of atrazine equivalents appearing in urine behave according to half-life of elimination functions as measured by Cheung (1990) 1, 2, 3, and 4 days after a single dose of atrazine.

The calculator requires the following information

- Duration of time since exposure (hours),
- Amount of urine in the sample (lites)
- Body weight (kilograms)
- Drinking water consumption rate (liters/day) and
- Inhalation rate (cubic meters of air/day)
- Dermal penetration (percent in 24 hours) (Forward-Calculator only).

For each a specified concentration of DACT, DEA or DEA in urine (ppb), the Back-Calculator determines the upper bound estimate of the

1. Amount of atrazine received (mg),
2. Atrazine dose (mg/kg),
3. Atrazine concentration in water (ppb), or
4. Atrazine concentration in air (μg/L).

The Calculator allows the user to specify the magnitude of any one of the four characteristics listed above, and then the magnitude of each of the other three characteristics are calculated.

2. Forward Calculator (Forward-Calc UrineConcALLroutes Worksheet)

This first worksheet **(Forward-Calc UrineConcALLroutes)** uses the data in Cheung (1990; See Worksheet 3 entitled Cheung (1990) to fit half-life of elimination models in order to predict the percent of atrazine equivalence concentration of DACT (Equation 1) , DEA (Equation 2) or DIA (Equation 3) appearing in human urine 1, 2, 3, and 4 days after the individual received a specified dose of atrazine. The half-life fitted models assume that the concentration of the chlorotriazine in the urine samples collected during the first 24 hours after dosing correspond to the concentration of a single urine sample 12 hours after dosing. Similarly, the concentration in the urine samples collected during the second 24 hours after dosing correspond to the concentration of a single urine sample at 36 hours after dosing, etc.

The models fit to the Cheung et al. (1990) data are as follows:

$$\%\,Atrazine\ Equivalence\ for\ DACT = 10.05 \times e^{-\ln(2) \times \frac{t}{13.75}} \qquad \textbf{Equation 1}$$

$$\%\,Atrazine\ Equivalence\ for\ DEA = 44.45 \times e^{-\ln(2) \times \frac{t}{3.89}} \qquad \textbf{Equation 2}$$

$$\%\,Atrazine\ Equivalence\ for\ DIA = 1.53 \times e^{-\ln(2) \times \frac{t}{16.92}} \qquad \textbf{Equation 3}$$

where t is the time in hours since the bolus dose of atrazine.

These equations are valid for times t greater than or equal 12 hours.

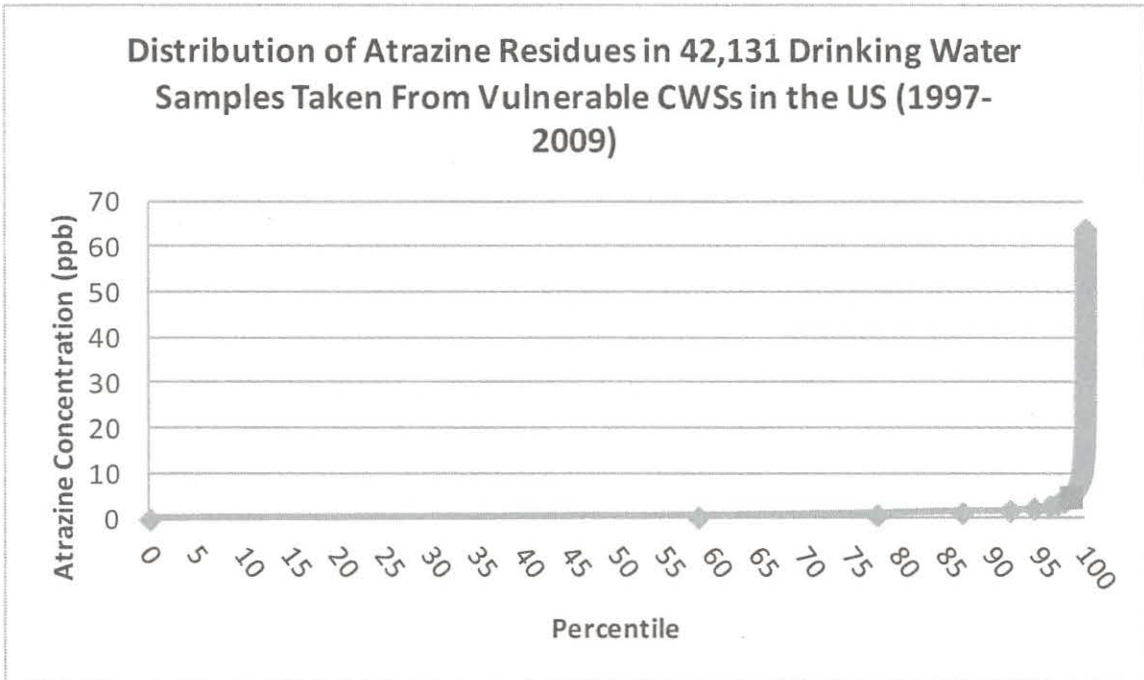
The Forward Calculator worksheet (Forward-Calc UrineConcALLroutes) allows the user to input exposure information for four routes of exposure [dietary, water ingestion, air inhalation and worker exposure (or dermal contact)]. The worksheet then calculates the urine concentrations of DACT, DEA and DIA in ppb at a specified number of hours after bolus dose exposure to atrazine.

The input and output to the Forward Calculator worksheet (Forward-Calc UrineConcALLroutes) are as shown in Figure 1.

> The user inputs are shown in green in Figure 1 (i.e., cells B3 through B18, and B20). The user can input any values he wishes in these cells. Default values are shown in cells A3 through A14 and A16.

Drinking Water Exposure

For B11, when the user specifies a value for the atrazine concentration (ppb) in drinking water, the adjacent sub-figure provides a reality check in that it shows where this input value is in the distribution of atrazine residues in 42,131 drinking water samples taken from vulnerable CWSs in the USA (1997-2009). For example, if the user inputs 5 ppb, then the sub-figure indicates that 5 ppb is in the upper tail of the distribution.



Exposure to Atrazine in Air

For B12, the user can specify any non-negative value for the atrazine concentration (μg/L) in air. Background information about observed atrazine concentrations (μg/L) in ambient air is in the worksheet "Ambient Air".

Dietary Exposure

For B13, the user can specify any non-negative value for dietary intake (mg of atrazine). The "Dietary Exposure Workshee" can be used to calculate dietary intake (mg of atrazine).

Worker/Dermal Exposure

For B14, the user can specify any non-negative value for worker exposure or intake from dermal contact.

If B14 ≤ 0, then the intake from dermal contact is calculated using the information in B15 through B21.

If B14 > 0, then B14 is the value for worker exposure.

Dermal Exposure Calculation

If B14 ≤ 0, then the intake from dermal contact is calculated using the information in B15 through B21. Specifically, the dermal exposure to atrazine (μg/cm^2) in B15 and percentage of dermal exposure absorbed (%) in B16 must be specified.

If B20 is non-negative (≥ 0), then

Dermal area exposed (m^2) (B21) = B20, and

Dermal intake (mg) (E28) = [Dermal exposure to atrazine ($\mu g/cm^2$) ((B15)]
x {[Percentage of dermal exposure absorbed (%) (B16)]/100}
x [Dermal area exposed (m^2) (B21)] x (10,000 cm^2 per m^2) x (0.001 mg per μg).

If B20 is negative (<0), then

Interpolated dermal area exposed (m^2) (B19) =
Specified percentile (B18) of the distributon of dermal area exposed corresponding to the specified Dermal Exposure Scenario (1, 2, 3, 4) (B17),

Dermal area exposed (m^2) (B21) = B19, and

Dermal intake (mg) (E28) = [Dermal exposure to atrazine ($\mu g/cm^2$) ((B15)]
x {[Percentage of dermal exposure absorbed (%) (B16)]/100}
x [Dermal area exposed (m^2) (B21)] x (10,000 cm^2 per m^2) x (0.001 mg per μg).

MLA-PHED

Background information about observed worker exposure values (mg/kg/day) is presented in the worksheet "MLA-PHED". In MLA-PHED, mg/kg/day are shown for Daily Dose, Annual Daily Dose, and Lifetime Average Daily Dose (LADD). Daily Dose refers to a day of application, mixing/loading, or flagging. Annual Daily Dose refers to averaging the dose from days of application, mixing/loading, or flagging in a year with zero for the rest of the days in that year. LADD refers to averaging the Annual Daily Dose for 35 years and zero for the other 35 years in a 70-year period.

Urinary Concentrations of DACT, DEA, and DIA

The urine concentrations of DACT, DEA, and DIA corresponding to the user-specified exposure inputs are in cells A30, A31, and A32. These totals, partitioned over routes (Water, Air Inhalation, Oral Ingestion, and Worker Exposure/Dermal) appear in cells B30, C30, D30, and E30 for DACT, B31, C31, D31, and E31 for DEA, and B32, C32, D32, and E32 for DIA. The attached bar graph shows the partitioning graphically for each source of exposure and each metabolite,

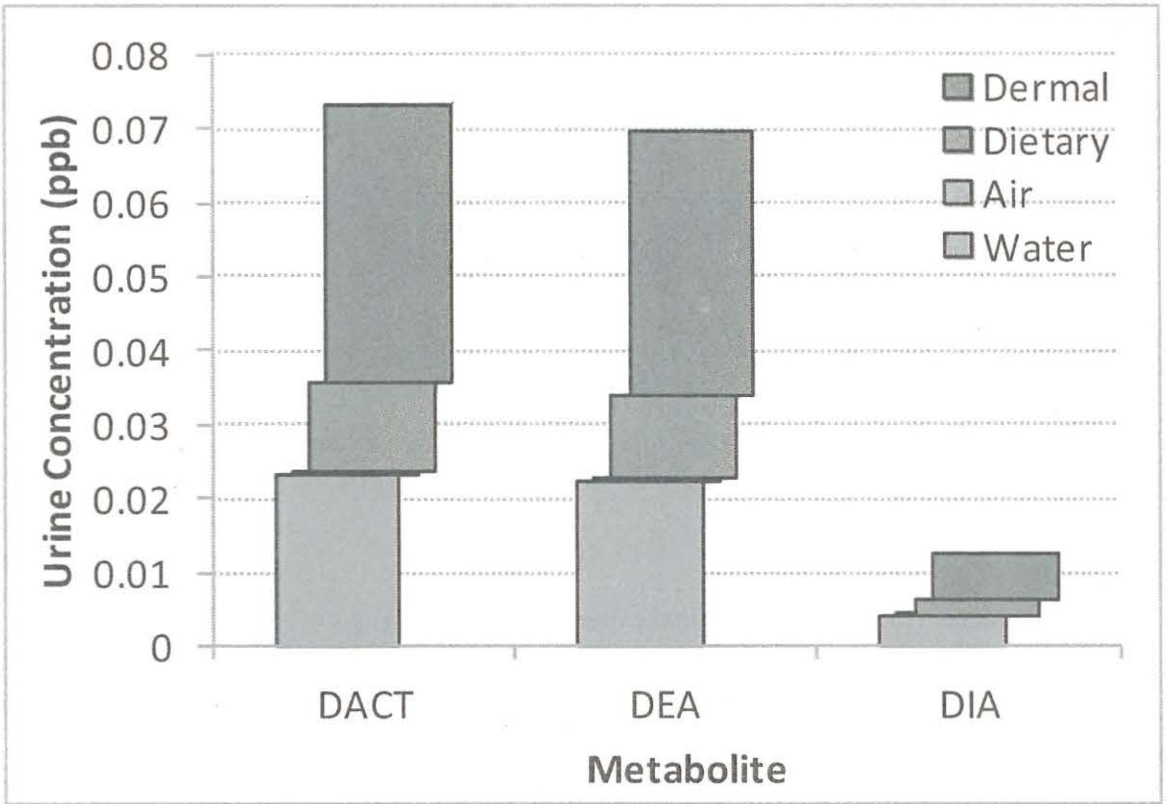
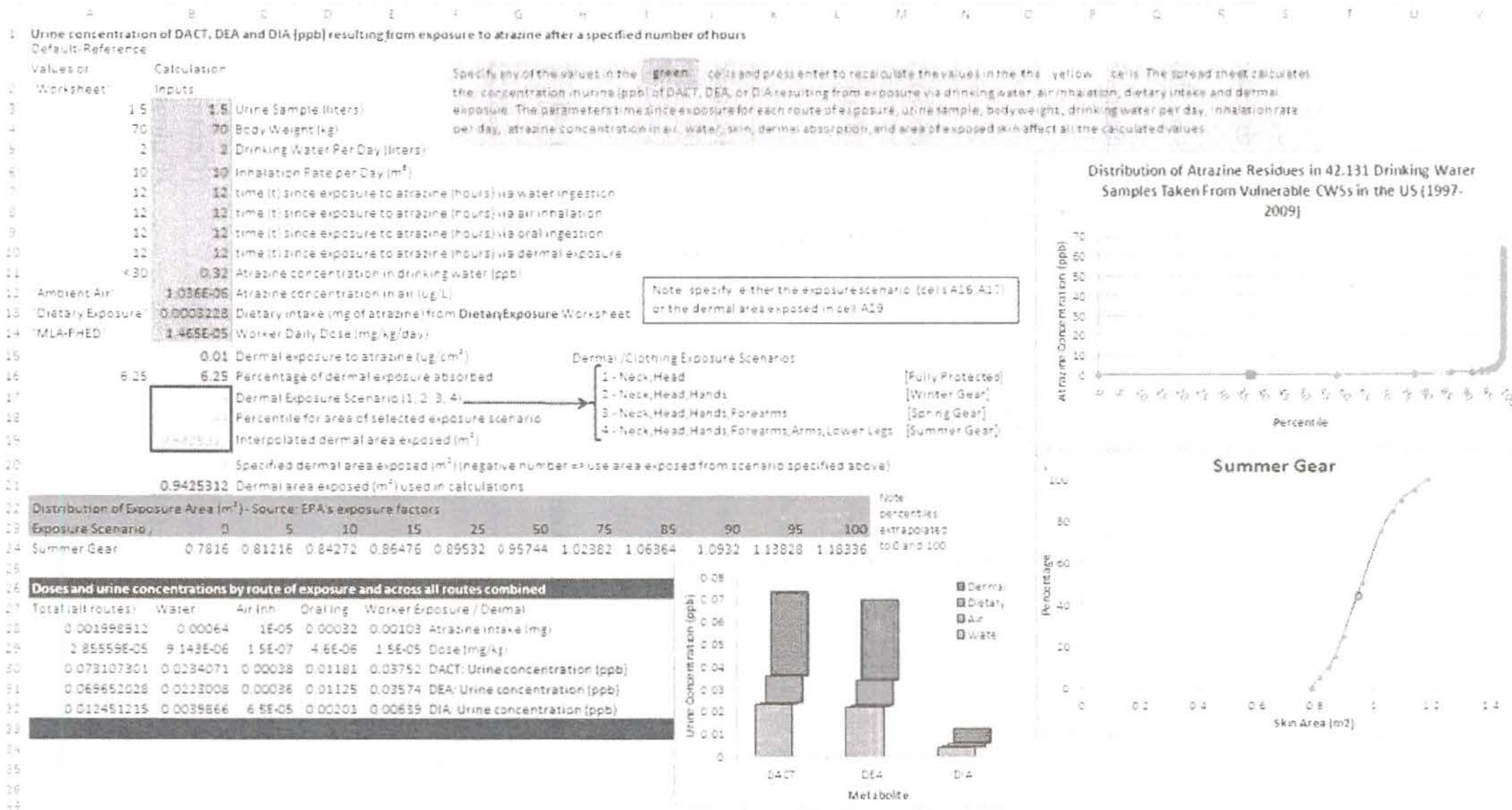

0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
Urine Concentration (ppb)
Dermal
Dietary
Air
Water
DACT
DEA
DIA
Metabolite

Figure 1. User-specified exposure information inputs for four routes of exposure [dietary, water ingestion, air inhalation and worker exposure (or dermal contact)] used to calculate the urine concentrations of DACT, DEA and DIA that would result after a specified number of hours from the time of the dosing



3. Back Calculator (Back-Calc HalfLifeHours Spreadsheet)

The second worksheet (**Back-Calc HalfLifeHours**) uses the data in Cheung (1990) as discussed for the Forward Calculator above.

Input to the Back-Calculator

Figure 2 shows the portion of the worksheet for entering the input into the Back Calculator.

The user is required to specify the following five general characteristics as shown in Figure 2.

1) Duration of time elapsed since exposure to the bolus dose of atrazine (hours)
2) Volume of urine sample (liters): Default = 1.5 liters)
3) Body weight (kilogram): Default = 70 kg for adult male
4) Amount of water consumed per day (liters): Default = 2 liters for adults
5) Volume of air consumed per day (Cubic meters): Default = 10 m^3

Duration of Time Since Exposure to Atrazine

The percent of atrazine equivalence for DACT, DEA and DIA are recalculated using the half-life equations given above every time a new time since exposure (Cell A20) is specified and the results are displayed in the yellow boxes indicated by arrow 6, 7 and 8 (cells J20, K20, and L20) for DACT, DEA, and DIA, respectively.

Back Calculation of the Atrazine Amount, Atrazine Dose, Water or Air Concentrations

Step 1: The user specifies inputs for variables 1 to 5 (Cells A20 to A24; Arrow Numbers 1 to 5) or accepts the defaults shown in Figure 2.

Step 2: The user specifies a urinary concentration of DACT (Cell B8), DEA (Cell C9) or DIA (Cell D10) (Arrow Numbers 9 to 11).

Step 3: The worksheet calculates the corresponding values for DACT (Row 8), DEA (Row 9), and DIA (Row 10):

- Amount of atrazine exposure (mg) (Column E)
- Atrazine dose (mg/kg) (Column F)
- Concentration of atrazine in water (ppb) (Column G)
- Concentration of atrazine in air (µg/liter) (Column H)

The user can also specify the following items/arrows 12 to 15 (i.e., cells E12, F14, G16, and H18) in the calculator as indicated below and shown in Figure 2.

Item/ Cell	User Specifies	Worksheet Calculates
12/ E12	amount of atrazine administered as a bolus dose (mg)	urine concentrations of DACT, DEA, DIA (ppb) atrazine dose (mg/kg) drinking water concentration (ppb) air concentration (μg/l)
13/ F14	atrazine dose (mg/kg)	urine concentrations of DACT, DEA, DIA (ppb) amount of atrazine administered as a bolus dose (mg) drinking water concentration (ppb) air concentration (μg/l)
14/ G16	drinking water concentration (ppb)	urine concentrations of DACT, DEA, DIA (ppb) amount of atrazine administered as a bolus dose (mg) atrazine dose (mg/kg) air concentration (μg/l)
15/ H18	air concentration (μg/l)	urine concentrations of DACT, DEA, DIA (ppb) amount of atrazine administered as a bolus dose (mg) atrazine dose (mg/kg) drinking water concentration (ppb)

Figure 3 shows the graphs corresponding to the equations of the percentage atrazine equivalence for DACT, DEA and DIA after a bolus dose of atrazine. The mean and 95% confidence intervals of the percent equivalence given by Cheung et al. (1990) are plotted along with the half-life equations fit to the data. A circle in the graphs indicates the percent atrazine equivalence corresponding to the time since bolus exposure specified in item 1 (cell A20) of Figure 2.

Figure 4 shows the atrazine dose (mg/kg), the amount of atrazine (mg), the maximum drinking water concentration of atrazine (ppb) and the maximum air concentration of atrazine (μg/L) for different times after dosing corresponding to specified urine concentrations of DACT, DEA and DIA. The urine concentrations (ppb) of DACT, DEA, and DIA are specified in row 44 (cells B44 for DACT, I44 for DEA, and P44 for DIA) of the worksheet Back-Calc HalfLifeHours.

Figure 2. Input section to the spreadsheet Back-Calc HalfLifeHours

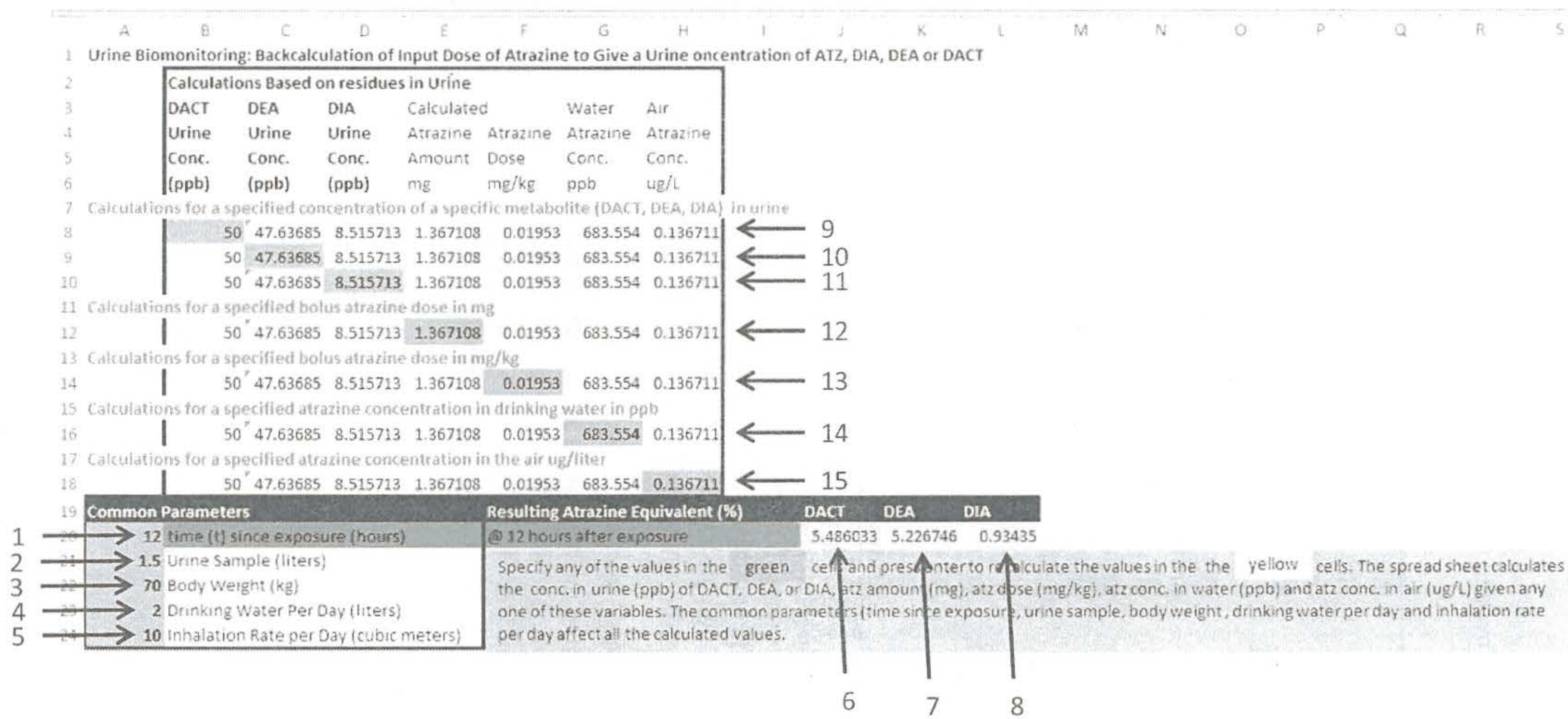


Figure 3. Graphs of the percent of atrazine equivalence for DACT, DEA and DIA after a bolus dose of atrazine in the spreadsheet Back-Calc HalfLifeHours derived from the Cheung et al. (1990) results reproduced in the worksheet "Data from Cheung (1990)"

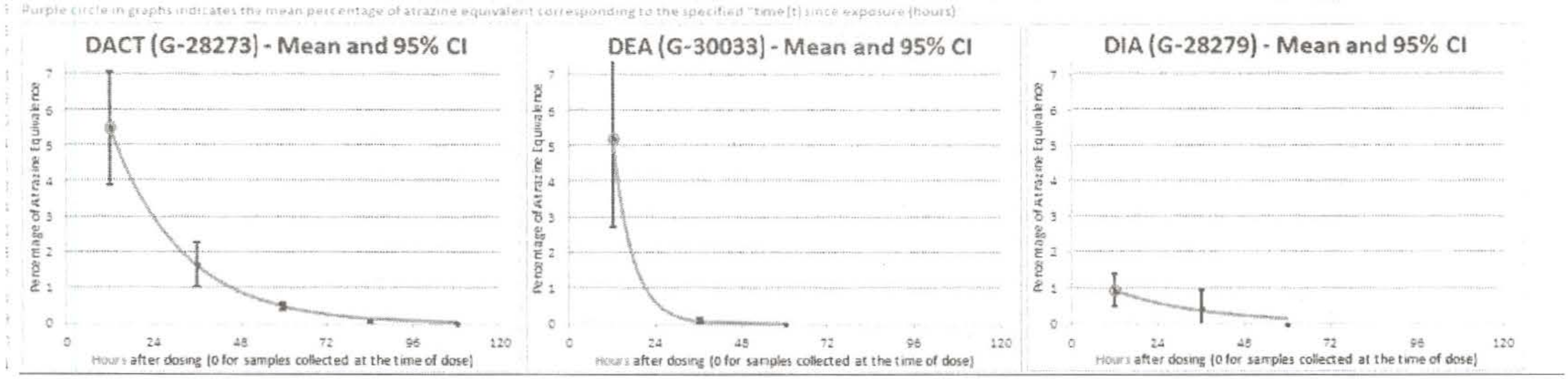


Figure 4. Output graphs showing the bolus doses in mg/kg, the bolus amounts in mg, and the maximum drinking water and air concentrations of atrazine corresponding to urine concentrations of DACT, DEA, and DIA specified in line 44 of the worksheet Back-Calc HalfLifeHours at different times since bolus dose and the parameters specified in items 1 to 5 (cells A20 to A24) discussed in Figure 2